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Long-Acting Drug Delivery Systems in 2026: From Extended Release to Patient-Centred Pharmacotherapy

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Abstract

Long-acting drug delivery systems are becoming increasingly important because they can maintain therapeutic exposure over weeks or months while reducing dosing frequency. The technology spans long-acting injectables, biodegradable microspheres, in situ depots, implants, transdermal systems and emerging long-acting formulations for peptides and biologics. A 2026 review of next-generation long-acting injectables highlights their potential to maintain drug levels for extended periods, improve adherence and reduce fluctuations in exposure. This article reviews the pharmaceutical principles behind long-acting delivery and argues that the next generation should focus not only on duration but also on predictability, reversibility, ease of administration, manufacturability and patient acceptability.

Keywords: Long-Acting Drug Delivery; Long-Acting Injectables; Sustained Release; Depot Systems; Microspheres; Adherence; Pharmaceutics

Introduction

Medication effectiveness depends not only on pharmacological activity but also on whether the medicine is taken correctly and consistently. Frequent dosing can create practical barriers, particularly in chronic disease. Long-acting drug delivery systems address this problem by maintaining drug exposure for extended periods while reducing administration frequency.

The concept is not new, but the technology is advancing rapidly. Current platforms include intramuscular and subcutaneous depot injections, biodegradable microspheres, implants, in situ forming depots, lipid-based systems and long-acting transdermal technologies. A 2026 review describes next-generation long-acting injectables as capable of maintaining more stable systemic exposure for weeks or months. [1] The pharmaceutical opportunity is to make these systems sufficiently predictable and patient-friendly for broader therapeutic use.

Why Long-Acting Delivery Matters

Conventional immediate-release products can produce peaks and troughs in plasma concentration. These fluctuations may contribute to adverse effects at high concentrations or inadequate efficacy at low concentrations. Sustained-release systems can flatten this profile and reduce the frequency of administration.

Reduced dosing frequency may also improve adherence. However, adherence should not be treated as an automatic benefit. A long-acting medicine may be easier to receive but harder to discontinue if adverse effects occur. Therefore, formulation design must balance persistence with controllability.

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Major Long-Acting Technologies

Long-acting injectable suspensions can use poorly soluble drug particles that dissolve gradually after administration. Polymeric microspheres, commonly based on biodegradable materials such as PLGA, can encapsulate a drug and release it as the matrix hydrates and degrades. In situ depots can form after administration and create a local reservoir. Lipid-based systems can improve solubility and control release for selected compounds.

Transdermal approaches use patches, microneedles or specialised materials to maintain drug input through the skin. Although not all of these systems are clinically mature, they represent an important direction for non-invasive long-acting therapy.

The Formulation Challenge: Predictable Release

The main challenge is not simply producing slow release. It is producing reproducible release. Small differences in particle size, polymer molecular weight, crystallinity, drug loading, injection site and manufacturing conditions can alter release kinetics.

For long-acting formulations, in vitro release testing must be meaningful enough to support formulation development and quality control. In vitro–in vivo relationships are particularly valuable because they can help connect laboratory release profiles with clinical exposure. Quality-by-design approaches can identify critical material attributes and process parameters that influence product performance.

Pharmacokinetic Advantages and Risks

A well-designed long-acting formulation can reduce peak-to-trough variability and maintain concentrations within a therapeutic window. This can be especially useful for drugs with short half-lives or where consistent exposure is clinically important.

However, long persistence can also create risks. If a patient develops an adverse reaction, the formulation cannot necessarily be removed. Drug accumulation may occur if dosing intervals are not correctly selected. Interpatient differences in absorption and depot behaviour may also be important. Consequently, long-acting products require careful pharmacokinetic modelling and clinical monitoring [1-2].

Patient-Centred Design

Pharmaceutical development should not define success solely as the longest possible duration. Patients may prefer a formulation that requires administration every month rather than every six months if it is easier to schedule or if discontinuation is important. Injection volume, needle size, injection-site reactions and administration setting can influence acceptability.

The best long-acting product is therefore the one that fits a real treatment pathway. Patient preferences, healthcare-worker workload and storage requirements should be considered alongside pharmacological performance.

Long-Acting Delivery for Peptides and Biologics

Peptides and proteins create additional challenges because they can be sensitive to aggregation, denaturation and chemical degradation. Long-acting delivery systems must protect molecular structure while maintaining biological activity.

This is an important frontier because many modern therapeutics have short systemic half-lives or require repeated administration. Depot systems, implants, encapsulation and specialised delivery materials may extend exposure without requiring structural modification of the active molecule. The formulation scientist therefore becomes a key contributor to therapeutic design rather than simply a downstream developer.

Manufacturing, Regulation and Scale-Up

A long-acting formulation that works in the laboratory is not automatically manufacturable at commercial scale. Mixing, particle formation, solvent removal, sterilisation and filling can affect product quality. Batch-to-batch consistency is essential because small differences may produce clinically meaningful changes in release.

Regulatory assessment must also consider dose proportionality, release kinetics, residual drug, impurities, device performance where applicable, and the consequences of delayed elimination. For complex products, analytical characterisation should be sufficiently detailed to explain performance rather than relying on a single release measurement.

Opinion: Duration Should Not Be the Only Goal

The next generation of long-acting delivery should be judged by a broader set of criteria: predictable exposure, patient acceptability, reversibility, safety, manufacturing robustness and affordability. A formulation that lasts one year but causes difficult injection-site reactions or cannot be

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reliably manufactured may have less practical value than a three-month formulation with excellent tolerability.

2026 research is increasingly focused on technological approaches that extend release while improving control [3-5]. This suggests that the field is moving from the simple idea of “slow release” toward engineered pharmacokinetic profiles.

Conclusion

Long-acting drug delivery is an important direction in modern pharmaceutics because it links formulation science with adherence, pharmacokinetics and patient-centred care. Advances in injectable depots, biodegradable microspheres, lipid systems, transdermal platforms and biologic formulations are expanding the possibilities. The central challenge is to achieve long duration without sacrificing predictability, safety or convenience. Future success will depend on integrated development in which formulation scientists, pharmacologists, clinicians, engineers and patients jointly define what an optimal long-acting medicine should achieve.

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